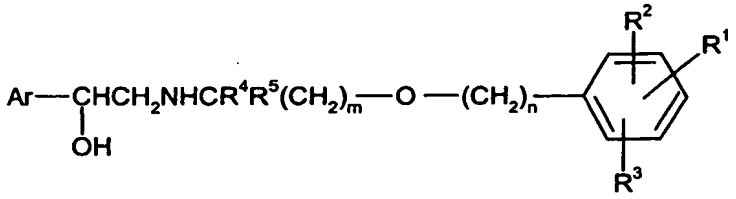
CLAIMS

1. A compound of formula (I):



(I)

or a salt, solvate, or physiologically functional derivative thereof, wherein:

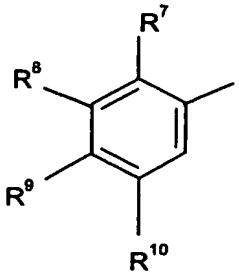
m is an integer of from 2 to 8; and
n is an integer of from 3 to 11;
with the proviso that m + n is 5 to 19;

R^1 is SR^6, SOR^6, or SO_2R^6,
wherein R^6 is a C_{3-7}cycloalkyl or C_{3-7}cycloalkenyl group;

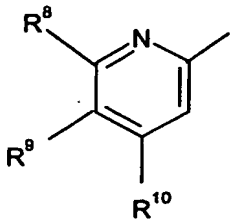
R^2 and R^3 are independently selected from hydrogen, C_{1-6}alkyl, C_{1-6}alkoxy, halo, phenyl, and C_{1-6}haloalkyl;

R^4 and R^5 are independently selected from hydrogen and C_{1-4}alkyl with the proviso that the total number of carbon atoms in R^4 and R^5 is not more than 4;

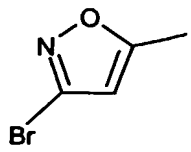
Ar is a group selected from



(a)

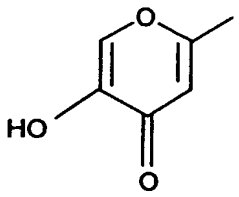


(b)



(c)

and



(d)

wherein R^8 represents hydrogen, halogen, $-(CH_2)_qOR^{11}$, $-NR^{11}C(O)R^{12}$, $-NR^{11}SO_2R^{12}$, $-SO_2NR^{11}R^{12}$, $-NR^{11}R^{12}$, $-OC(O)R^{13}$ or $OC(O)NR^{11}R^{12}$,
and R^7 represents hydrogen, halogen, or C_{1-4} alkyl;

or R^8 represents $-NHR^{14}$ and R^7 and $-NHR^{14}$ together form a 5- or 6- membered heterocyclic ring;

R^9 represents hydrogen, halogen, $-OR^{11}$ or $-NR^{11}R^{12}$;

R^{10} represents hydrogen, halogen, haloC_{1-4} alkyl, $-OR^{11}$, $-NR^{11}R^{12}$, $-OC(O)R^{13}$ or $OC(O)NR^{11}R^{12}$;

R^{11} and R^{12} each independently represents hydrogen or C_{1-4} alkyl, or in the groups $-NR^{11}R^{12}$, $-SO_2NR^{11}R^{12}$ and $-OC(O)NR^{11}R^{12}$, R^{11} and R^{12} independently represent hydrogen or C_{1-4} alkyl or together with the nitrogen atom to which they are attached form a 5-, 6- or 7- membered nitrogen-containing ring,

R^{13} represents an aryl (eg phenyl or naphthyl) group which may be unsubstituted or substituted by one or more substituents selected from halogen, C_{1-4} alkyl, hydroxy, C_{1-4} alkoxy or halo C_{1-4} alkyl; and

q is zero or an integer from 1 to 4.

2. A compound of formula (I) or a salt, solvate of physiologically functional derivative thereof, wherein formula (I) is as defined in claim, except that R^8 does not represent hydrogen.

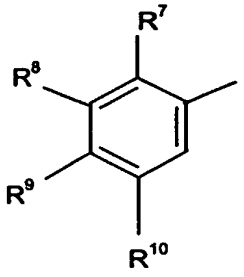
3. A compound according to claim 1 or claim 2 wherein R^1 represents $-SO_2R^6$.

4. A compound according to any of claims 1 to 3 wherein R^6 represents a C_{3-7} cycloalkyl group.

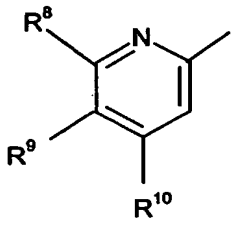
5. A compound according to any of claims 1 to 4 wherein R^2 and R^3 each represent hydrogen.

6. A compound according to any of claims 1 to 5 wherein R^4 and R^5 are independently selected from hydrogen and methyl.

7. A compound according to any of claims 1 to 6 wherein Ar is selected from a group (a) or (b):

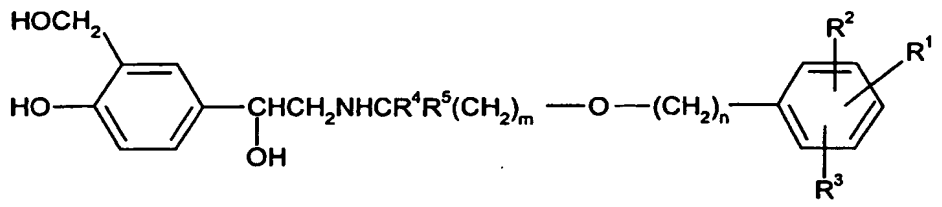


(a)



(b)

8. A compound of formula (Ia):



(Ia)

or a salt, solvate, or physiologically functional derivative thereof, wherein:

m is an integer of from 2 to 8; and
n is an integer of from 3 to 11;
with the proviso that m + n is 5 to 19;

R^1 is SR^6, SOR^6, or SO_2R^6,
wherein R^6 is a C_{3-7}cycloalkyl or C_{3-7}cycloalkenyl group;

R^2 and R^3 are independently selected from hydrogen, C_{1-6}alkyl, C_{1-6}alkoxy, halo, phenyl, and C_{1-6}haloalkyl; and

R^4 and R^5 are independently selected from hydrogen and C_{1-4}alkyl with the proviso that the total number of carbon atoms in R^4 and R^5 is not more than 4.

9. A compound according to any of claims 1 to 8 wherein m is 5 or 6 and n is 3 or 4.

10. A compound of formula (I) or (Ia) selected from:
4-{(1*R*)-2-[(6-{4-[3-(Cyclopentylsulfinyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol;
4-{(1*R*)-2-[(6-{4-[3-(Cyclopentylsulfinyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol (Isomer 1);
4-{(1*R*)-2-[(6-{4-[3-(Cyclopentylsulfinyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol (Isomer 2);
4-{(1*R*)-2-[(6-{4-[3-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol;
4-{(1*R*)-2-[(6-{4-[4-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol;

4-((1*R*)-2-{[6-({4-[3-(Cyclohexylsulfonyl)phenyl]butyl}oxy)hexyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;
4-((1*R*)-2-{[6-({4-[3-(3-Cyclopenten-1-ylsulfonyl)phenyl]butyl}oxy)hexyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;
4-((1*R*)-2-{[6-({5-[3-(Cyclopentylsulfonyl)phenyl]pentyl}oxy)hexyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;
4-((1*R*)-2-{[7-({3-[3-(Cyclopentylsulfonyl)phenyl]propyl}oxy)heptyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;
4-((1*R*)-2-{[6-({4-[3-(Cyclopentylsulfonyl)-5-methylphenyl]butyl}oxy)hexyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;
N-[5-((1*R*)-2-{[6-({4-[3-(Cyclopentylsulfonyl)phenyl]butyl}oxy)hexyl]amino}-1-hydroxyethyl)-2-hydroxyphenyl]methanesulfonamide;
4-((1*R*)-2-{[6-({4-[3-(Cyclopentylsulfonyl)phenyl]butyl}oxy)hexyl]amino}-1-hydroxyethyl)-2-fluorophenol;
6-{2-[(6-{4-[3-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)pyridin-3-ol;
5-{(1*R*)-2-[(6-{4-[3-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-8-hydroxy-3,4-dihydroquinolin-2(1*H*)-one;
5-{(1*R*)-2-[(6-{4-[3-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-hydroxyphenylformamide;
and salts, solvates, and physiologically functional derivatives thereof.

11. A compound of formula (I) or (Ia) which is:
4-{(1*R*)-2-[(6-{4-[3-(Cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol;
or a salt, solvate, or physiologically functional derivative thereof.

12. A compound according to any of claims 1 to 11 in the form of a salt formed with an arylsulphonic acid.

13. A compound according to any of claim 8, claim 9 or claim 12 which is selected from:
4-{(1*R*)-2-[(6-{4-[3-(cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl) phenol 4-methylbenzenesulfonate;
4-{(1*R*)-2-[(6-{4-[3-(cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol 4-bromobenzene sulfonate;

4-{(1*R*)-2-[(6-{4-[3-(cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol 4-chlorobenzene sulfonate
4-{(1*R*)-2-[(6-{4-[3-(cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol 3-toluene sulfonate;
4-{(1*R*)-2-[(6-{4-[3-(cyclopentylsulfonyl)phenyl]butoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl) phenol 4-biphenyl sulfonate; and
4-{(1*R*)-2-[(6-{4-[3-(cyclopentylsulfonyl)phenyl]butoxy} hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol, naphthalene-2-sulfonate.

14. A compound according to claim 13 wherein the salt is in crystalline form.

15. A method for the prophylaxis or treatment of a clinical condition in a mammal, such as a human, for which a selective β_2-adrenoreceptor agonist is indicated, which comprises administration of a therapeutically effective amount of a compound of formula (I) or (Ia) according to any of claims 1 to 14 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof.

16. A compound of formula (I) or (Ia) according to any of claims 1 to 14 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof for use in medical therapy.

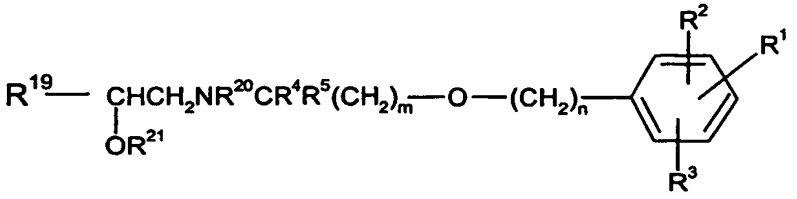
17. A pharmaceutical formulation comprising a compound of formula (I) or (Ia) according to any of claims 1 to 14 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof, and a pharmaceutically acceptable carrier or excipient, and optionally one or more other therapeutic ingredients.

18. A combination comprising a compound of formula (I) or (Ia) according to any of claims 1 to 14 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof, and one or more other therapeutic ingredients.

19. The use of a compound of formula (I) or (Ia) according to any of claims 1 to 14 or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof in the manufacture of a medicament for the prophylaxis or treatment of a clinical condition for which a selective β_2-adrenoreceptor agonist is indicated.

20. A process for the preparation of a compound of formula (I) or (Ia) according to any of claims 1 to 14 or a salt, solvate, or physiologically functional derivative thereof, which comprises:

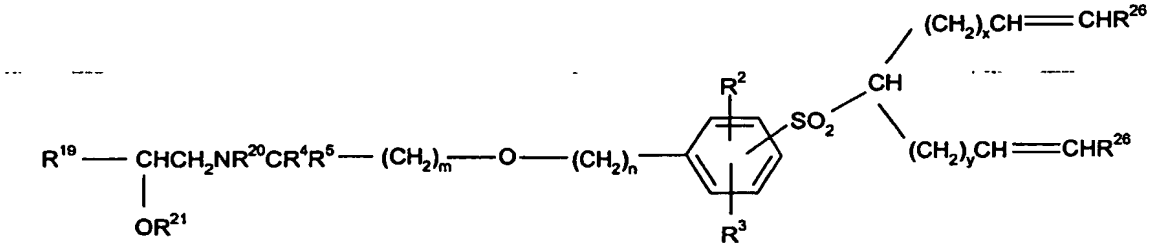
(a) deprotection of a protected intermediate, for example of formula (II):



(II)

or a salt or solvate thereof, wherein R^1, R^2, R^3, R^4, R^5, m, and n are as defined for the compound of formula (I), R^{19} represents an optionally protected form of Ar; and R^{20} and R^{21} are each independently either hydrogen or a protecting group, provided that the compound of formula (II) contains at least one protecting group;

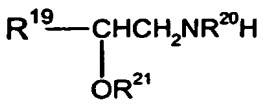
(b) reaction of a compound of formula (X):



(X)

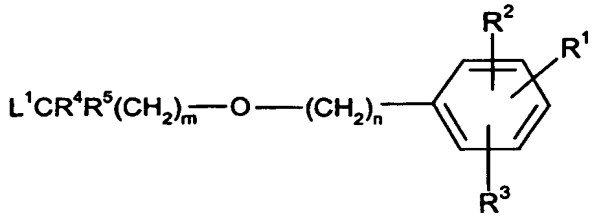
wherein R^2, R^3, R^4, R^5, R^{19}, R^{20}, R^{21}, m and n are as defined for formula (II) each R^{26} independently represents hydrogen or C_{1-4}alkyl, and x and y each represent 0, 1 or 2; to effect ring closure;

(c) alkylation of an amine of formula (XIII):



(XIII)

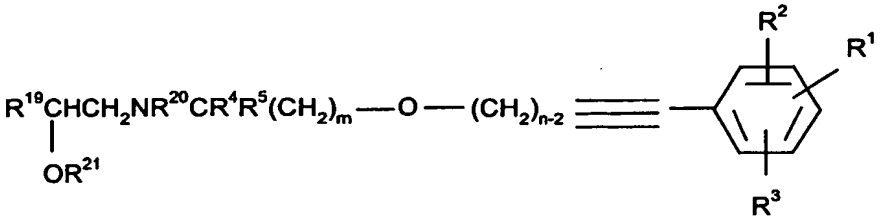
wherein R^{22}, R^{23}, R^{20} and R^{21} are each independently either hydrogen or a protecting group with a compound of formula (XVII):



(XVII)

wherein R^1, R^2, R^3, R^4, R^5, m, and n are as defined for the compound of formula (I) and L^1 is a leaving group;

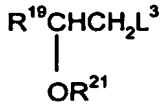
(d) reduction of a compound of formula (XIX):



(XIX)

Wherein R^1, R^2, R^3, R^4, R^5, m and n are as defined for formula (I), R^{19} represents an optionally protected form of Ar and R^{20} and R^{21} are each independently hydrogen or a protecting group as defined above.

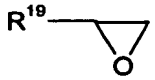
(e) reacting a compound of formula (XXIII):



(XXIII)

wherein R^{19} is as hereinbefore defined and L^3 is a leaving group as defined above for L^1 or L^2;

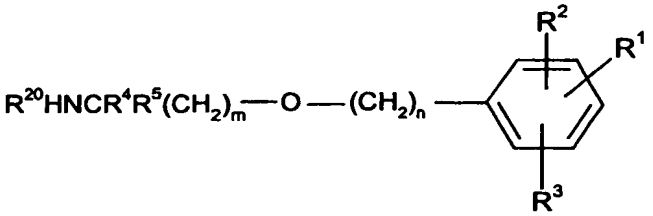
or a compound of formula (XXIV):



(XXIV)

wherein R^{19} is as hereinbefore defined

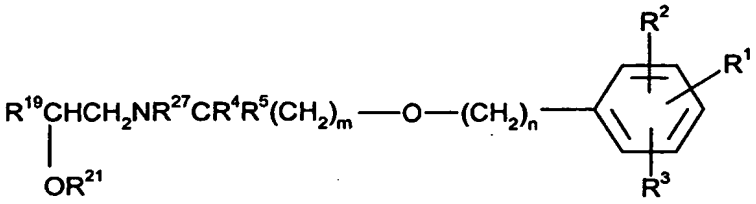
with an amine of formula (XXV):



(XXV)

wherein R^1, R^2, R^3, R^4, R^5, R^{20}, m and n are as defined for formula (II); or

(f) removal of a chiral auxiliary from a compound of folrmula (IIa)



(IIa)

wherein R^1 – R^5, m and n are as defined for formula (I), R^{19} represents an optionally protected form of Ar, R^{21} represent hydrogen or a protecting group and R^{27} represents a chiral auxiliary.

followed by the following steps in any order:

(i) optional removal of any protecting groups;

(ii) optional separation of an enantiomer from a mixture of enantiomers;

(iii) optional conversion of one compound of formula (I) to a different compound of formula (I) eg. conversion of a compound wherein R^1 is SR^6 to a compound wherein R^1 is SOR^6 or SO_2R^6, or conversion of a compound wherein R^1 is SOR^6 to a compound wherein R^1 is SO_2R^6;

(iv) optional conversion of a compound wherein R^6 represents cycloalkenyl to a compound wherein R^6 represents cycloalkyl, eg. by hydrogenation;

(v) optional conversion of the product to a corresponding salt, solvate, or physiologically functional derivative thereof.

21. An intermediate selected from a compound of formula (II) (III) (IV) (X) and (XIX) as hereinbefore defined.